MANDAMINE

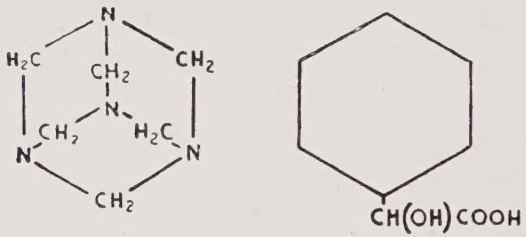
FOR URINARY ANTISEPSIS

'MANDAMINE'

The right combination

'MANDAMINE' combines in one distinct chemical compound the antibacterial actions of two valuable urinary antiseptics—mandelic acid and methenamine (hexamine). It retains the potent antiseptic qualities of these drugs but eliminates the disadvantages which attend them when given separately.

'Mandamine' may be structurally illustrated as:—



$C_{14}H_{20}O_3N_4$; molecular weight 292·33

Extensive experimental and clinical investigations have established the bactericidal effectiveness of 'Mandamine' against a wide range of organisms commonly met with in urinary tract infections, particularly against the frequently encountered *B. coli* and *Staphylococcus aureus*.[1]

A PROMPT AND CONVENIENT TREATMENT

Early control of infection is the characteristic response to 'Mandamine'. The urine becomes microscopically and culturally negative in an average of six days;[1] however, the drug is non-cumulative in action and may, if necessary, be administered over long periods.

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In a discussion of 'Mandamine' in their authoritative work, *Clinical Urology*, Lowsley and Kirwin[2] state that the urine will often be cleared of organisms in from 3 to 5 days, although in certain cases it has been necessary to persist with the treatment for a longer period.

Dietary restriction and control of fluid intake are unnecessary with 'Mandamine',[1,2,3] and this absence of restriction is generally found to be a significant contribution toward the convenience of the treatment.

LACK OF TOXICITY

The impressive lack of toxicity shown by 'Mandamine' facilitates treatment and simplifies the task of selecting patients. The evidences of intoxication so often seen when using other forms of mandelic acid—nausea, vomiting, and gastro-intestinal discomfort—have not been observed by investigators into 'Mandamine' treatment.[2] Carroll and Allen[1] conclude that the drug is virtually non-toxic in therapeutic dosage. The absence of toxicity makes 'Mandamine' especially suitable for use during pregnancy, for children, and in stubborn or inoperable cases where treatment is necessarily prolonged.

The only major contra-indication to 'Mandamine' is renal insufficiency.

THERAPEUTIC ACTIVITY OF 'MANDAMINE'

Bacterial Resistance

In the selection of a urinary antiseptic an important consideration must be the likelihood of bacterial resistance developing to the chosen medicament. Studies by Duca

and Scudi[4] show that many organisms causing urinary tract infections prove or become resistant to sulphathiazole and streptomycin. In contrast, resistance to 'Mandamine' either does not occur, or appears slowly and to a questionable degree. Further, the same organisms which resist sulphathiazole and streptomycin remain fully susceptible to 'Mandamine'. This conclusion is confirmed by Almquest and Titus,[5] who note that resistance sometimes develops to the sulphonamides, but that 'Mandamine' treatment 'often affords excellent results in *bacillus coli*, streptococcus and staphylococcus infections of the urinary tract.'

Helmholz and Alford[6] found that strains of *B. coli* resistant to sulphathiazole were also resistant to urinary acidity and mandelic acid, but were readily susceptible to 'Mandamine'.

Urinary pH

Supplementary acidification of urine is normally unnecessary with 'Mandamine' treatment. The drug invariably lowers the urinary pH and maintains a state of desirable acidity.[3] Carroll and Allen[1] report that in 192 out of 200 patients treated with 'Mandamine' the urine became or remained acid without other medication.

The pH changes produced by bacteria in some cases lead to striking increases in alkalinity, but in the presence of adequate concentrations of 'Mandamine' these same organisms produce no significant alteration in the urinary pH.

Some urinary tract infections are caused by urea-splitting bacteria, which so increase the alkalinity of the urine that the infections do not respond readily to 'Mandamine' alone. These cases require accessory acidification of the urine over a period of 24 to 36 hours, after which 'Mandamine' can adequately assume control of the urinary pH[10].

Bactericidal Action

'Mandamine' is remarkably effective in pyelitis, pyelonephritis, cystitis, prostatitis, urethro-trigonitis, and infections complicating renal calculi and bladder disturbances of nervous origin. Disturbing urinary symptoms are usually alleviated rapidly, and in the absence of obstruction the urine is promptly cleared of organisms in a high percentage of cases.

In a controlled study carried out by Carroll and Allen[1] of 200 unselected cases of common urinary infections, approximately 74% of the patients responded to routine 'Mandamine' therapy.

By far the most frequently encountered organism in this study was *B. coli*, which accounted for 104 infections. The response to 'Mandamine' of 85·6% of the patients was evidenced by negative cultures and clinical relief.

Staphylococcus aureus accounted for a further 28 infections, and 71·4% of these were similarly relieved by 'Mandamine'.

The prevailing organisms in the Kirwin and Bridges[7] series of 63 patients were *B. coli*, streptococcus, and staphylococcus. Altogether 83% of the total number of patients responded favourably to the treatment. In 24 patients the urine cleared with negative cultures for *B. coli*, *Staphylococcus albus*, and non-haemolytic streptococcus within 3 to 5 days, and in 28 cases the urine cleared and the cultures became negative after more extended trial.

Carroll, Allen, and Doubly[8] reported a controlled study of 39 patients with infections of the urinary tract caused by *B. pyocyaneus*. Using a variety of drugs, they conclude that penicillin and the sulphonamide compounds are relatively

ineffective against this bacillus. Streptomycin gave good results, but the frequent occurrence of bacterial resistance led the authors to conclude that mandelic acid or 'Mandamine' was a preferable medicament.

CLINICAL STUDIES

Pyelitis

In 45 patients suffering from pyelitis[1] the response to 'Mandamine' treatment was outstandingly good. Thirty-eight patients showed negative urine cultures, some in as short a time as 3 days. Abnormal temperatures subsided, and a normal degree of acidity was restored and maintained in the urine.

Pyelitis sometimes complicates pregnancy. At such a time it entails a risk to life and also gives rise to chronic ill-health. It is common experience that pyelitis of pregnancy with its accompanying urinary stasis frequently proves resistant to treatment, and that the urine rarely becomes sterile before delivery. 'Mandamine' may be confidenlty prescribed because it does not aggravate the nausea of pregnancy and because of its certain and effective bactericidal action. Pieri[9] recommends its use because it seldom causes irritation of the urinary tract and may be administered safely over long periods.

Cystitis

Carroll and Allen[1] report 26 cases of cystitis and Kirwin and Bridges[7] 18. Uniformly good results were obtained with 'Mandamine' treatment in both trials. In the first series 22 patients showed negative urine cultures, and a correspondingly high percentage of patients were relieved in the second series.

The majority of cases of pyelitis or cystitis with prostatic hypertrophy reported by the authors[1,7] showed marked improvement with 'Mandamine' treatment.

Urinary Infections in Children

'Mandamine' has proved effective in these cases, provided there is satisfactory renal function and no obstruction in the urinary tract. Successful results may be expected in a large percentage of children with acute, recurrent, or chronic urinary infections.

DOSAGE

The average daily dose for adults is three or four tablets three times daily; for children in proportion. Infants under one year of age may be given one tablet, twice daily, crushed and dissolved in milk or sweetened water.

SUMMARY

It is evident that no one drug can be universally successful in all urinary tract infections. The sulphonamides, though often valuable, have an unpredictable toxicity which constitutes a definite limitation to their use.[1,10] Streptomycin frequently and rapidly produces bacterial resistance.[4] Penicillin, brilliantly successful in many serious disorders, failed to destroy the organisms responsible for the majority of cases studied by Carroll and Allen.[1] 'Mandamine' however, is peculiarly free from restrictions which usually complicate urogenital therapy, and consequently provides a safe, simple, and effective treatment in a wide range of urinary tract infections.

'Mandamine' is the registered trade mark of Nepera Chemical Co. Inc., New York

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'Mandamine' is supplied in enteric-coated tablets of 0·25 *g.* (3¾ *gr.*) *each, in bottles of* 60, 500 *and* 1000

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